IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
KLAUS HELLERBRAND et al.

Application No.: 10/598,698 | Confirmation No.: 9077

Filed: September 8, 2006 | Art Unit:1628

For: COATED IMPLANTS, THEIR MANUFACTURING AND USE THEREOF | Examiner: DENNIS HEYER

APPEAL BRIEF

MS Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

May 10, 2012

Dear Sir:

Appellants submit this Appeal Brief in accordance with 37 C.F.R. § 41.37 in support of their appeal from the Final Office Action, mailed October 19, 2011 by Examiner Dennis Heyer, and the Advisory Action, mailed January 27, 2012, in the above-identified patent application.

In accordance with 37 C.F.R. §§ 41.31 and 41.37, this Appeal Brief follows the March 12, 2012 filing of a Notice of Appeal and payment of the required fee. Appellants submit that this Appeal Brief is timely filed within two months of the March 12, 2012 Notice of Appeal, is in furtherance of said Notice of Appeal, and is accompanied by the required fee. The filing of this Appeal Brief requires no extension of time fee. However, the Commissioner is hereby authorized to charge any unpaid fees deemed required in connection with this Appeal Brief, or to credit any overpayment, to Deposit Account No. 50-5256.

The fees required under 37 C.F.R § 41.20(b)(2) are also dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This brief contains items under the following headings as required by 37 C.F.R. § 41.37 and M.P.E.P. § 1205.2:

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I. REAL PARTY IN INTEREST

The real party in interest for this appeal is SCIL Technology GmbH.

The inventors assigned all their respective rights in and to this application to SCIL Technology GmbH, as recorded under Reel/Frame 018250/0380 on September 14, 2006.

II. RELATED APPEALS AND INTERFERENCES

To Appellants' knowledge, there are no other appeals, interferences or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

A. Total Number of Claims in Application

Claims 1, 4, 6, 8-9, 11-17, 48, and 51-54 are pending in the present application.

B. Current Status of Claims

1. Claims canceled: 2-3, 5, 7, 18-47 and 49-50
2. Claims withdrawn from consideration but not canceled: none
3. Claims pending: 1, 4, 6, 8-9, 11-17, 48, and 51-54
4. Claims allowed: none
5. Claims rejected: 1, 4, 6, 8-9, 11-17, 48, and 51-54

C. Claims On Appeal

The claims on appeal are claims 1, 4, 6, 8-9, 11-17, 48, and 51-54.

IV. STATUS OF AMENDMENTS

No amendments have been filed subsequent to the mailing of the October 19, 2011 Final Office Action.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The present invention relates to a method of coating of a device, preferably implants, with a substance comprising the steps of (a) contacting said device with a solution of said substance or substrate, and (b) drying said device while being in contact with said solution (Specification, page 1, lines 8-11). The present invention also relates to a packaging container for a device, preferably an implant, said packaging container being adapted such that said device is coatable within said packaging container (Specification, lines 11-13).

Independent claim 1 recites a "method of coating of a device with a substance comprising the steps of" (Specification, page 5, lines 15-16) "(a) providing a container having a receptacle for receiving the device to be coated" (Specification, page 23, line 2; page 24, lines 1-2), "wherein the receptacle of the container is coaxially located within a container housing" (Specification, page 24, lines 14-15), "the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container" (Specification, page 23, lines 30-32, page 24, lines 2-4 and 17-21), "wherein an inner surface

of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device" (Specification, page 24, lines 4-6 and lines 10-12); "(b) providing a solution of the coating substance within the receptacle" (Specification, page 23, lines 2-3 and page 24, lines 15-19); "(c) inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed" (Specification, page 23, lines 3-5 and page 24, lines 15-19); and "(d) starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance" (Specification, page 19, line 33-34, page 20, lines 6-25, page 21, lines 4-10, and page 23, lines 5-8 and lines 17-28).

Independent claim 54 recites a "method of coating of a device with a substance comprising the steps of" (Specification, page 5, lines 15-16) "(a) providing a container having a receptacle for receiving the device to be coated" (Specification, page 23, line 2; page 24, lines 1-2), "wherein the receptacle of the container is coaxially located within a container housing" (Specification, page 24, lines 14-15), "the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container" (Specification, page 23, lines 30-32, page 24, lines 2-4 and 17-21), "wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device" (Specification, page 24, lines 4-6 and lines 10-12), "and wherein the container and the receptacle is a packaging container for the device" (Specification, page 23, line 30 to page 24, line 4); "(b) providing a solution of the coating substance within the receptacle" (Specification, page 23, lines 2-3 and page 24, lines 15-19); "(c) inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed" (Specification, page 23, lines 3-5 and page 24, lines 15-19); and "(d) starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance" (Specification, page 19, line 33-34, page 20, lines 6-25, page 21, lines 4-10, and page 23, lines 5-8 and lines 17-28).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether claims 1, 4, 6, 8, 11-12, 16-17 and 54 can properly be rejected as obvious under 35 U.S.C. § 103(a) on a combination of Song, PCT Published Application No. WO 2005/016399 A1 ("Song") in view of Klokkers-Bethke et al., U.S. Patent No. 5,335,769 ("Klokkers-Bethke"), Talalay, U.S. Patent No. 4,063,367 ("Talalay"), and Graff, U.S. Patent No. 5,316,146 ("Graff").

2. Whether claims 9, 13, 48 and 52-53 can properly be rejected as obvious under 35 U.S.C. § 103(a) on a combination of Song in view of Klokkers-Bethke, Talalay and Graff, as applied to claims 1, 4, 6, 8, 11-12, 16-17 and 54, and further in view of Kohnert et al., PCT Published Application No. WO 2003/043673 ("Kohnert").

3. Whether claim 15 can properly be rejected as obvious under 35 U.S.C. § 103(a) on a combination of Song in view of Klokkers-Bethke, Talalay and Graff, as applied to claims 1, 4, 6, 8, 11-12, 16-17 and 54, and further in view of Lee et al., U.S. Patent No. 5,571,523 ("Lee").

4. Whether claim 51 can properly be rejected as obvious under 35 U.S.C. § 103(a) on a combination of Song in view of Klokkers-Bethke, Talalay and Graff, as applied to claims 1, 4, 6, 8, 11-12, 16-17 and 54, and further in view of Gao et al., U.S. Patent No. 6,113,993 ("Gao").

VII. ARGUMENT

Grounds of Rejection No. 1: Obvious rejection of claims 1, 4, 6, 8, 11-12, 16-17 and 54 based on a combination of Song, Klokkers-Bethke, Talalay and Graff"

Song describes a method of making a medical device comprising (a) providing a solution comprising (i) solvent, (ii) a therapeutic agent, and (iii) an antioxidant; (b) providing a medical device substrate; (c) contacting the solution with the medical device substrate; and (d) removing the solvent from the solution to form the therapeutic-agent-containing region.

The therapeutic-agent-containing region can be formed by dipping the medical device substrate into the solution followed by drying to remove the solvent. Song describes that the therapeutic-agent containing region can be dried after formation to remove the solvent species. Song describes that subsequent to its formation, the medical device can be placed in a non-oxidizing environment such as packaging that has been evacuated or into which an inert gas has been introduced. See Song, page 2, paragraph [0012], page 11, paragraph [0042], page 12, paragraphs [0045] to [0047] and page 13, paragraph [0051].

Klokkers-Bethke describes a method of in situ freeze-drying a solution containing a solid product in a solvent. A liquid solution comprising a solid product dissolved in a solvent is added to a glass container having its inside surface coated with a silicone material. The container with the liquid solution is subjected to acceptable operation conditions of temperature and reduced pressure to remove the solvent by freeze drying so as to leave the solid product in the container in the form of a dense compact coherent solid. The container is sealed by means which maintain the solid product stable over a useful storage shelf life. See Klokkers-Bethke, column 1, lines 10-14, column 3, lines 10-22.

Talalay describes a method for rapidly drying liquid-solid composites and biologically active material in situ in a container. Containers are filled with a solution and placed on a conveyor which moves through a pre-drying housing or tunnel where ambient or gently warmed air is blown over the surface of the solution in the containers. The containers are then introduced into a chamber having a high vacuum on the order of about 500 microns in the chamber to complete the drying operation. The chamber is then filled with an inert gas such as nitrogen at a pressure slightly greater than atmospheric while the containers are sealed. A dry, positively sealed container of biologically active material which is not friable and which is well adhered to the wall of the container in which it is dried is thereby provided. See Talalay, column 1, lines 38-50, 57-59, column 2, lines 2-7, column 3, lines 22-25, column 4, lines 55-68 and column 6, lines 45-48.

Graff describes a transport container for transporting fragile articles such as test tubes or vials. The transport container comprises a first body member including a spring for providing an axial bias force to a vial supported therewith for restraining movement of the vial in a first axial direction and for urging the vial toward a second body member for proper seating therein. The second body member includes a plurality of positioning vanes which provide a yieldable restraint in a second axial direction. The first and second body members

are connected to form a releasable, liquid-tight seal and joint therebetween. See Graff, the Abstract and Figs. 1 and 1a.

Independent claim 1 recites a "method of coating of a device with a substance comprising the steps of:

(a) providing a container having a receptacle for receiving the device to be coated, wherein the receptacle of the container is coaxially located within a container housing, the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container, wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device;

(b) providing a solution of the coating substance within the receptacle;

(c) inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed; and

(d) starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance."

Step (a) of independent claim 1 therefore requires that a container having a receptacle for receiving the device to be coated be provided. Said receptacle of the container must be coaxially located within a container housing. The container and the receptacle must be configured so that the device is coatable with the coating substance directly in the container. An inner surface of the receptacle must be coated with a layer of an inert, repelling material. The inert repelling material must increase a quantitative deposition of the coating substance on the device. Step (b) requires that a solution of the coating substance be provided within the receptacle. Step (c) requires that the device be inserted into the solution of the coating substance within the receptacle of the container. Steps (b) and (c) can be reversed. Step (d) requires that isothermal drying of the device be started while the device remains within the solution held within the receptacle of the container. Volatile components must thereby be removed from the solution of the coating substance.

Independent claim 54 recites the additional limitation in step (a) "wherein the container and the receptacle is a packaging container for the device". Said additional

limitation therefore requires that the container and the receptacle must be a packaging container for the device.

Applicants respectfully submit that none of Song, Klokkers-Bethke, Talalay and Graff teach or suggest, either alone or in combination, all of the aforementioned features of independent claim 1 of the present invention. Specifically:

Step a) of independent claim 1 requires:

> "providing a container having a receptacle for receiving the device to be coated, wherein the receptacle of the container is coaxially located within a container housing, the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container, wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device"

Applicants respectfully submit that none of Song, Klokkers-Bethke, Talalay or Graff teach or suggest "providing a container having a receptacle for receiving the device to be coated". Graff at best discloses a transport container 10 for a test tube or vial 60. See Graff, column 4, lines 41-42 and Fig. 1. While never specifically disclosing a container or a receptacle, Song does discloses a "dipping technique" which has been interpreted by the Office to require some sort of container/receptacle. See Office Action of October 19, 2011, Detailed Action, page 6, lines 1-11. However, Song fails to disclose that the container has a receptacle as is required by independent claim 1. Each of Klokkers-Bethke, Talalay and Graff fail to teach or suggest a device. None of Song, Klokkers-Bethke, Talalay or Graff teach or suggest "the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container." None of Song, Klokkers-Bethke, Talalay or Graff teach or suggest that "an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device." Only Klokkers-Bethke teaches a device with an inert, repelling material, that being silicon. See Klokkers-Bethke, column 2, lines 54-60 and column 3, lines 26-32 and 53-57. However Klokkers-Bethke fails to teach or suggest that said inert, repelling material is configured to increase a quantitative deposition of the coating substance on the device because, as stated above, Klokkers-Beth nowhere teaches a device. Klokkers-Bethke at best teaches that a

compact coherent lycophilizate cake can be obtained. See Klokkers-Bethke, column 4, Table 1 (see "+"). Klokkers-Bethke does, not, however, teach or suggest that a quantitative deposition of the coating substance on the device is increased, which feature is summarized by Fig. 9 of the present application. Talalay teaches away from this feature by requiring it to be essential that the material be well adhered to the container (the tray in Talalay), a result the present application seeks to avoid. See Talalay, column 1, lines 42-47 and column 6, lines 45-48.

Step b) of independent claim 1 requires:

"providing a solution of the coating substance within the receptacle"

Applicants respectfully submit that none of Song, Klokkers-Bethke, Talalay or Graff teach or suggest "providing a solution of the coating substance within the receptacle". Neither Klokkers-Bethke, Talalay or Graff teach or suggest a coating substance at all. If Song is interpreted to teach the aforementioned feature by virtue of its teaching of dipping, Song would then, however, necessarily fail to teach or suggest a "providing a container having a receptacle" as required in step a) above.

Step c) of independent claim 1 requires:

"inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed"

Applicants respectfully submit that none of Song, Klokkers-Bethke, Talalay or Graff teach or suggest "inserting the device into the solution of the coating substance within the receptacle of the container". Klokkers-Bethke, Talalay and Graff each fail to teach or suggest a device or a coating substance at all. Song at best discloses a "dipping technique", but fails to disclose that said dipping (coating) occurs "within the receptacle of the container" as is required by independent claim 1. Furthermore, none of Song, Klokkers-Bethke, Talalay or Graff teach or suggest reversing the order of steps (b) and (c); i.e., first c) "inserting the device into the solution of the coating substance within the receptacle of the container," and then b) "providing a solution of the coating substance within the receptacle". Song at best

teaches dipping which would require that the solution already exist in the container or receptacle.

Step d) of independent claim 1 requires:

> "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance"

Applicants respectfully submit that none of Song, Klokkers-Bethke, Talalay or Graff teach or suggest "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance." The Office cites Talalay as describing an isothermal drying step. See Office Action of October 19, 2011, Detailed Action, page 10, lines 7-13. The Office has stated that the isothermal drying step is disclosed on page 20, lines 6-25 of the present specification where it is stated that the process is carried out under reduced pressure and at a defined (constant) temperature. Talalay does not, however, specifically describe these conditions and therefore does not describe an isothermal drying step at all. In contrast, Talalay only describes that in step 1, "the temperature is kept to approximately 65° C or below". See Talalay, column 3, lines 56-58. No defined (constant) temperature is thereby taught or suggested. With respect to the temperatures in steps 2 and 3, Talalay never describes any temperature conditions at all. Applicants can only assume that if warm dried air is used in tunnel 23, that a different temperature (i.e., air which is not warmed or dried) is used in sealing assembly 29 where steps 2 and 3 are performed. However, Talalay simply does not disclose this information. No isothermal drying step of the present application is therefore taught or suggested by Talalay.

With respect to the additional limitation of independent claim 54, none of Song, Klokkers-Bethke, Talalay and Graff teach or suggest that "the container and the receptacle is a packaging container for the device."

Applicants note that the Office currently requires four references, 1) Song, 2) Klokkers-Bethke, 3) Talalay and 4) Graff, in order to make the present rejection of independent claims 1 and 54. With respect to the primary reference, Song, the Office admits that Song does not explicitly teach the following limitations:

- Step (a) which requires that the receptacle into which the medical device is dipped be coaxially located within a container housing;
- Step (a) which requires that the inner surface of the receptacle be coated with a layer of an inert repelling material configured to increase a quantitate deposition of the coating substance on the device; and
- Step (d) which requires that isothermal drying of the device be started while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance.

See Office Action of October 19, 2011, Official Action, page 7, lines 12 to page 8, line 1. Song at best teaches that a medical device can be: 1) dipped into a mixture containing a therapeutic agent, antioxidant and/or polymer dissolved in a solvent; 2) removed and, after formation; 3) dried (in an oven). See Song, paragraphs [0040], [0042], [0045] and [0051]. However, the Office states that:

> It would have been *prima facie* obvious to one of ordinary skill in the art, at the time the invention was made, to modify the oven drying step taught by Song to alternatively, dry the device by removing volatile components from the solution of the coating substance while the device is held in a coating solution within a receptacle that becomes a packaging container.
>
> **One would have been motivated to do so** because starting drying by the method of Klokkers-Bethke (i.e. freeze-drying under reduced vacuum in an inert atmosphere) while the device is held in a coating solution within a receptacle followed by sealing said receptacle such that it becomes a packaging container **minimizes exposure of the coated device to an oxidizing atmosphere** which, as taught be Klokkers-Bethke, provides stability to the dried product allowing for a useful storage shelf life. Further, **Song explicitly teaches the desirability of limiting exposure of the coated medical device to an oxidizing atmosphere** by maintaining it in an inert atmosphere ("it may be beneficial to maintain a therapeutic agent coated onto a medical device in a **non-oxidizing environment during the course of its formation**, Song, page 12, p [0046] and [0047] and, encourages placing the coated medical device into packaging (a receptacle) that has been evacuated or into which an inert gas (e.g.

> nitrogen) has been introduced **in order to maintain a non-oxidizing environment** (Song, p [0047]).
>
> Accordingly, modifying the drying (dipping) step of Song such that the solvent is removed while the device remains in the coating solution and wherein receptacle becomes the packaging container by the freeze drying and sealing steps of Klokkers-Bethke, both of which are carried out under vacuum and in a nitrogen atmosphere, would avoid the step of transferring the coated device from a potentially oxidizing atmosphere to a "package" that contains an inert atmosphere.

Emphasis added. See Office Action of October 19, 2011, Official Action, page 7, line 12 to page 13, line 1. The Office therefore states that it is *prime facie* obvious to modify the teaching of Song by applying the drying method of Klokkers-Bethke based on the motivation of minimizing exposure to an oxidizing environment. While the drying method of Klokkers-Bethke might reduce exposure to oxygen, it does not completely eliminate it. Klokkers-Bethke describes that the ampoules are placed into a chamber which is then flooded with nitrogen. The ampoules are therefore originally in an oxygen-containing environment. See Klokkers-Bethke, column 4, lines 28-30. Applicants respectfully submit that a person skilled in the art with the motivation of minimizing exposure to an oxidizing environment would therefore not have combined Song with Klokkers-Bethke. However, even if such a combination were made, the Office admits that the combination of Song with Klokkers-Bethke fails to teach the required limitation of removing the solvent by isothermal drying as recited in claim 1, step (d). See Office Action of October 19, 2011, Official Action, page 10, lines 1-5 (the Office also admits that Klokkers-Bethke does not teach step (a) which requires that the receptacle into which the medical device is dipped be coaxially located within a container housing). In seeking to incorporate this limitation, the Office substitutes the freeze-drying step of Klokkers-Bethke for the "isothermal-drying" step of Talalay. The motivation therefor is stated to be as follows:

> One would have been motivated to do so because Talalay teaches isothermal drying **allows one to seal the receptacle** (container) following removal of moisture (liquid) an thus ensure a longer shelf life of the material contained within.

Emphasis Added. See Office Action of October 19, 2011, Official Action, page 14, lines 7-10. Applicants respectfully submit that a person skilled in the art would never have made such a substitution for at least the three following reasons:

Firstly, the motivation offered by the Office to replace the drying method of Klokkers-Bethke with that of Talalay, allowing one to seal the receptacle following removal of moisture to ensure a longer shelf life of the material contained therein, is already solved by Klokkers-Bethke. Klokkers-Bethke specifically states that after freeze-drying, the container is sealed so as to maintain the solid products over a useful storage shelf life. See Klokkers-Bethke, column 3, lines 20-22. The Office in fact points out that Klokkers-Bethke provides a sealing step which allows for a useful shelf life. See Office Action of October 19, 2011, Official Action, page 12, lines 17-22. Applicants therefore submit that a person skilled in the art would not be motivated to resolve a non-existing "problem" because the problem had already been solved.

Secondly, the motivation offered by the Office to combine Song with Klokkers-Bethke, the desirability of limiting exposure of the coated medical device to an oxidizing atmosphere, would be destroyed if the Talalay drying method were performed. Talalay describes a three-step drying process. Containers (trays 18 with wells 19a) are first filled with a solution and placed on a conveyor which moves through a pre-drying housing or tunnel 23 under the influence of vibrators 24 and 25 where ambient or gently warmed air is blown over the surface of the solution in the containers via conduit 35. See Talalay, column 1, line 53 to column 2, line 2, column 3, lines 49-60 and Figs. 1 and 4. In a second step, the containers are introduced into a chamber (sealing assembly 29) having a high vacuum on the order of about 500 microns in the chamber to complete the drying operation. See Talalay, column 2, lines 2-4 and column 4, lines 50-60. None of the aforementioned first two steps are, however, undertaken in an inert atmosphere. Only after these two steps are finished, and the drying process completed, is the chamber filled in a third step with an inert gas such as nitrogen at a pressure slightly greater than atmospheric while the containers are sealed. See Talalay, column 2, lines 4-5. All drying steps in Talalay therefore occur in an oxygen environment. Incorporating the Talalay drying method would therefore increase exposure of the coated medical device to an oxidizing atmosphere, particularly since warmed, oxygen-containing air is passed via conduit 35 over the enlarged effective surface area of the liquid in each well created by the vibration. The substitution of the Talalay drying process therefore runs

contrary to the stated motivation for combining Song with Klokkers-Bethke in the first place, that being to limit exposure of the coated medical device to oxygen.

Thirdly, as already set forth above, Applicants submit that Talalay does not describe an isothermal drying step as required by the present invention. The Office has correctly stated that the isothermal drying step is disclosed on page 20, lines 6-25 of the present specification where it is stated that the process is carried out under reduced pressure and at a defined (constant) temperature. Talalay does not, however, specifically describe these conditions and therefore does not describe an isothermal drying step at all. Talalay only describes that in step 1, "the temperature is kept to approximately 65° C or below". See Talalay, column 3, lines 56-58. No defined (constant) temperature is thereby taught or suggested. With respect to the temperatures in steps 2 and 3, Talalay never describes any temperature conditions at all. Applicants can only assume that if warm dried air is used in tunnel 23, that a different temperature (i.e., air which is not warmed or dried) is used in sealing assembly 29 where steps 2 and 3 are performed. However, Talalay simply does not disclose this information. No isothermal drying step of the present application is therefore taught or suggested by Talalay.

Summarizing the aforementioned, the Office has presented a motivation to combine Song with Klokkers-Bethke, that motivation being to minimize exposure of the medical device to an oxidizing environment. The Office then substituted a freeze-drying step in Klokkers-Bethke for an "isothermal drying" step in Talalay. The motivation presented for said substitution was to allow sealing of the receptacle (container) to ensure a longer shelf life of the contained material. The substitution of the freeze-drying step in Klokkers-Bethke with the "isothermal drying" step in Talalay, however, will increase exposure of the medical device to an oxidizing environment and wholly contradict the stated motivation of combining Song with Klokkers-Bethke in the first place. A failure to substitute the drying step of Klokkers-Bethke will that of Talalay will, however, result in the absence of the required isothermal drying limitation. The stated motivation for substituting the drying steps, however, also does not exist because Klokkers-Bethke already provides for a sealing of the receptacle (container) to ensure a longer shelf life of the contained material. Talalay furthermore does not even provide an isothermal drying step. A person of ordinary skill in the art would therefore never have combined Song, Klokkers-Bethke and Talalay.

Applicants further respectfully submit that the Office has here failed to make even a *prima facie* case of obviousness. The Office has failed to resolve the level of ordinary skill in

the pertinent art as the United States Supreme Court required in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). See MPEP 2141. Applicants further submit that, once the level of ordinary skill in the pertinent art has been resolved, that the Office must then then provide a rational underpinning for a person of ordinary skill in the art to Song, Klokkers-Bethke, Talalay and Graff; the United States Supreme Court having held that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See MPEP 2142 and 2143.01 IV. The required articulated reasoning with some rational underpinning has not here been made because the Office has not resovled the level of ordinary skill in the pertinent art.

Because each of Song, Klokkers-Bethke, Talalay and Graff are missing at least the aforementioned recited elements as recited in independent claims 1 and 54, it is respectfully submitted that any combination of Song, Klokkers-Bethke, Talalay and Graff, to the extent proper, could not render either of independent claims 1 and 54, nor their dependent claims, obvious.

Accordingly, it is respectfully submitted that claims 1, 4, 6, 8, 11-12, 16-17 and 54 are patentable over a combination of Song, Klokkers-Bethke, Talalay and Graff.

Grounds of Rejection No. 2: Obvious rejection of claims 9, 13, 48 and 52-53 based on a combination of Song, Klokkers-Bethke, Talalay, Graff and Kohnert

Song, Klokkers-Bethke, Talalay and Graff were described above.

Kohnert describes a device having osteoinductive and osteoconductive properties in vivo comprising a carrier containing calcium phosphate and an osteoinductiv protein. The device is prepared by providing a solution comprising an osteoinductive protein and a buffer and contacting the solution with a carrier containing calcium phosphate. See Kohnert, page 6, line 27 to page 7, line 4 and the Abstract.

It is respectfully submitted that each of claims 9, 13, 48 and 52-53 properly depend from independent claim 1. As stated above, each of Song, Klokkers-Bethke, Talalay and Graff fail to teach or suggest all the features recited by independent claim 1. A person of

ordinary skill in the art would also never have combined Song, Klokkers-Bethke and/or Talalay for the reasons set forth above. Kohnert does not cure this defect. Kohnert describes a device having osteoinductive and osteoconductive properties in vivo comprising a carrier containing calcium phosphate and an osteoinductiv protein. The device is prepared by providing a solution comprising an osteoinductive protein and a buffer and contacting the solution with a carrier containing calcium phosphate. See Kohnert, page 6, line 27 to page 7, line 4 and the Abstract. However, Kohnert nowhere teaches or suggests the aforementioned recited limitations of independent claim 1. Merely as an example, Kohnert nowhere teaches or describes the required limitation of "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance."

Applicants further respectfully submit that the Office has here failed to make even a *prima facie* case of obviousness. The Office has failed to resolve the level of ordinary skill in the pertinent art as the United States Supreme Court required in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). See MPEP 2141. Applicants further submit that, once the level of ordinary skill in the pertinent art has been resolved, that the Office must then then provide a rational underpinning for a person of ordinary skill in the art to Song, Klokkers-Bethke, Talalay, Graff and Kohnert; the United States Supreme Court having held that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See MPEP 2142 and 2143.01 IV. The required articulated reasoning with some rational underpinning has not here been made because the Office has not resovled the level of ordinary skill in the pertinent art.

Because each of Song, Klokkers-Bethke, Talalay, Graff and Kohnert are missing at least the aforementioned recited elements as recited in independent claim 1, it is respectfully submitted that any combination of Song, Klokkers-Bethke, Talalay, Graff and Kohnert, to the extent proper, could not render independent claim 1, nor any of its dependent claims 9, 13, 48 and 52-53, obvious.

Accordingly, it is respectfully submitted that claims 9, 13, 48 and 52-53 are patentable over a combination of Song, Klokkers-Bethke, Talalay, Graff and Kohnert.

Grounds of Rejection No. 3: Obvious rejection of claim 15 based on a combination of Song, Klokkers-Bethke, Talalay, Graff and Lee

Song, Klokkers-Bethke, Talalay and Graff were described above.

Lee describes a method of inhibiting arteriosclerosis or smooth muscle cell proliferation by identifying an animal having an artery suspected of needing inhibition and contacting the artery with an apoptosis-inducing amount of an antioxidant such as methionine. See Lee, column 1, lines 37-40 and the Abstract.

It is respectfully submitted that claim 15 properly depends from independent claim 1. As stated above, each of Song., Klokkers-Bethke, Talalay and Graff fail to teach or suggest all the aforementioned features of independent claim 1. A person of ordinary skill in the art would also never have combined Song, Klokkers-Bethke and/or Talalay for the reasons set forth above. Lee does not cure this defect. In contrast, Lee only describes a method of inhibiting arteriosclerosis or smooth muscle cell proliferation by identifying an animal having an artery suspected of needing inhibition and contacting the artery with an apoptosis-inducing amount of an antioxidant such as methionine. See Lee, column 1, lines 37-40 and the Abstract. However, Lee nowhere teaches or suggests the aforementioned recited limitations of independent claim 1. Merely as an example, Lee nowhere teaches or describes the required limitation of "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance."

Applicants further respectfully submit that the Office has here failed to make even a *prima facie* case of obviousness. The Office has failed to resolve the level of ordinary skill in the pertinent art as the United States Supreme Court required in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). See MPEP 2141. Applicants further submit that, once the level of ordinary skill in the pertinent art has been resolved, that the Office must then then provide a rational underpinning for a person of ordinary skill in the art to Song, Klokkers-Bethke, Talalay, Graff and Lee; the United States Supreme Court having held that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385,

1396 (2007) quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See MPEP 2142 and 2143.01 IV. The required articulated reasoning with some rational underpinning has not here been made because the Office has not resovled the level of ordinary skill in the pertinent art.

Because each of Song, Klokkers-Bethke, Talalay, Graff and Lee are missing at least the aforementioned recited elements as recited in independent claim 1, it is respectfully submitted that any combination of Song, Klokkers-Bethke, Talalay, Graff and Lee, to the extent proper, could not render independent claim 1, nor its dependent claim 15, obvious.

Accordingly, it is respectfully submitted that claim 15 is patentable over a combination of Song, Klokkers-Bethke, Talalay, Graff and Lee.

Grounds of Rejection No. 4: Obvious rejection of claim 51 based on a combination of Song, Klokkers-Bethke, Talalay, Graff and Gao

Song, Klokkers-Bethke, Talalay and Graff were described above.

Gao teaches a method of coating a substrate with a calcium phosphate compound using plasma enhanced MOCVD. The substrate can thereby be a titanium alloy. See Gao, column 3, lines 4-8 and the Abstract.

It is respectfully submitted that claim 51 properly depends from independent claim 1. As stated above, each of Song, Klokkers-Bethke, Talalay and Graff fail to teach or suggest the aforementioned features recited in independent claim 1. A person of ordinary skill in the art would also never have combined Song, Klokkers-Bethke and/or Talalay for the reasons set forth above. Gao does not cure this defect. In contrast, Gao only describes a method of coating a substrate with a calcium phosphate compound using plasma enhanced MOCVD. See Gao, column 3, lines 4-8 and the Abstract. However, Gao nowhere teaches or suggests the aforementioned recited limitations of independent claim 1. Merely as an example, Gao nowhere teaches or describes the required limitation of "starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance."

Applicants further respectfully submit that the Office has here failed to make even a *prima facie* case of obviousness. The Office has failed to resolve the level of ordinary skill in the pertinent art as the United States Supreme Court required in Graham v. John Deere Co.,

383 U.S. 1, 148 USPQ 459 (1966). See MPEP 2141. Applicants further submit that, once the level of ordinary skill in the pertinent art has been resolved, that the Office must then then provide a rational underpinning for a person of ordinary skill in the art to Song, Klokkers-Bethke, Talalay, Graff and Gao; the United States Supreme Court having held that "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." KSR International Co. v. Teleflex Inc., 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007) quoting In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See MPEP 2142 and 2143.01 IV. The required articulated reasoning with some rational underpinning has not here been made because the Office has not resovled the level of ordinary skill in the pertinent art.

Because each of Song, Klokkers-Bethke, Talalay, Graff and Gao are missing at least the aforementioned recited elements as recited in independent claim 1, it is respectfully submitted that any combination of Song, Klokkers-Bethke, Talalay, Graff and Gao, to the extent proper, could not render independent claim 1, nor its dependent claim 51, obvious.

Accordingly, it is respectfully submitted that claim 51 is patentable over a combination of Song, Klokkers-Bethke, Talalay, Graff and Gao.

VIII. CLAIMS

A copy of the claims involved in the present appeal is attached hereto as **Appendix A**.

CONCLUSION

For all of the reasons set forth above, the rejections of claims 1-26 should be reversed. Appellants respectfully request that the rejections be withdrawn, and the case passed to allowance.

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Respectfully submitted,

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Attachments: Appendices A, B, and C

APPENDIX A

Claims Involved in the Appeal of Application Serial No. 10/598,698

Listing of Claims:

Claim 1 (Previously Presented): Method of coating of a device with a substance comprising the steps of:

(a) providing a container having a receptacle for receiving the device to be coated, wherein the receptacle of the container is coaxially located within a container housing, the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container, wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device;

(b) providing a solution of the coating substance within the receptacle;

(c) inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed; and

(d) starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance.

Claims 2-3 (Cancelled)

Claim 4 (Previously Presented): The method of claim 1, wherein said substance is a pharmaceutically active substance.

Claim 5 (Cancelled)

Claim 6 (Previously Presented): The method of claim 4, wherein said pharmaceutically active substance is immobilized in an inorganic or organic bioresorbable material.

Claim 7 (Cancelled)

Claim 8 (Previously Presented): The method of claim 1, wherein said substance comprises nonactive ingredients.

Claim 9 (Previously Presented): The method of claim 1, wherein said substance comprises calcium phosphates.

Claim 10 (Cancelled)

Claim 11 (Previously Presented): The method of claim 1, wherein the container becomes a packaging container for the device.

Claim 12 (Previously Presented): The method of claim 1, wherein said solution is an aqueous solution or an organic solvent.

Claim 13 (Previously Presented): The method of claim 1, wherein said solution is an acid aqueous solution.

Claim 14 (Previously Presented): The method of claim 1, wherein said solution contains an antioxidant.

Claim 15 (Original): The method of claim 14, wherein said antioxidant is methionin or its derivatives.

Claim 16 (Previously Presented): The method of claim 1, wherein said device is made of metal or metal alloy.

Claim 17 (Previously Presented): The method of claim 1, wherein said device is a dental implant or a coronary stent.

Claims 18-47 (Cancelled)

Claim 48 (Previously Presented): The method of claim 1, wherein the method provides a homogeneous distribution of the coating on the device.

Claims 49-50 (Cancelled)

Claim 51 (Previously Presented): The method of claim 1, wherein said device is made of titanium or a titanium alloy.

Claim 52 (Previously Presented): The method of claim 1, wherein said device is made of calcium phosphate.

Claim 53 (Previously Presented): The method of claim 1, wherein said device is made of ß-tricalcium phosphate.

Claim 54 (Previously Presented): Method of coating of a device with a substance comprising the steps of:

(a) providing a container having a receptacle for receiving the device to be coated, wherein the receptacle of the container is coaxially located within a container housing, the container and the receptacle being configured so that the device is coatable with the coating substance directly in the container, wherein an inner surface of the receptacle is coated with a layer of an inert, repelling material configured to increase a quantitative deposition of the coating substance on the device, and wherein the container and the receptacle is a packaging container for the device;

(b) providing a solution of the coating substance within the receptacle;

(c) inserting the device into the solution of the coating substance within the receptacle of the container, where the order of steps (b) and (c) can be reversed; and

(d) starting isothermal drying of the device while the device remains within the solution held within the receptacle of the container, thereby removing volatile components from the solution of the coating substance.

APPENDIX B

No evidence pursuant to 37 C.F.R. §§ 1.130, 1.131, or 1.132 or entered by or relied upon by the examiner is being submitted.

APPENDIX C

No related proceedings are referenced in II. above, hence copies of decisions in related proceedings are not provided.